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NEWS 14 AUG 18 Data available for download as a PDF in RDISCLOSURE  
NEWS 15 AUG 18 Simultaneous left and right truncation added to PASCAL  
NEWS 16 AUG 18 FROSTI and KOSMET enhanced with Simultaneous Left and Right  
Truncation  
NEWS 17 AUG 18 Simultaneous left and right truncation added to ANABSTR  
NEWS 18 SEP 22 DIPPR file reloaded  
NEWS 19 SEP 25 INPADOC: Legal Status data to be reloaded  
  
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```
=> e guerin marchand claudine/au
E1      1      GUERIN MARCHAND/AU
E2      65     GUERIN MARCHAND C/AU
E3      18 --> GUERIN MARCHAND CLAUDINE/AU
E4      2      GUERIN MARCHAND GLAUDINE/AU
E5      4      GUERIN MARIANNE/AU
E6      2      GUERIN MARIE A/AU
E7      1      GUERIN MARIE ANDREE/AU
E8      46     GUERIN MARIE CHRISTINE/AU
E9      2      GUERIN MARIE F/AU
E10     10     GUERIN MARIE FRANCE/AU
E11     1      GUERIN MARIE LUCE/AU
E12     1      GUERIN MARIE T/AU
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=> s el-e4
L1      86 ("GUERIN MARCHAND"/AU OR "GUERIN MARCHAND C"/AU OR "GUERIN MARCH
AND CLAUDINE"/AU OR "GUERIN MARCHAND GLAUDINE"/AU)
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=> e druilhe pierre/au
E1      813    DRUILHE P/AU
E2      5      DRUILHE P */AU
E3      121 --> DRUILHE PIERRE/AU
E4      25     DRUILHE R/AU
E5      10     DRUILHE RAYMOND/AU
E6      51     DRUILHET A/AU
E7      6      DRUILHET AIME/AU
E8      3      DRUILHET B/AU
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E9 2 DRUILHET BOB/AU  
 E10 1 DRUILHET P/AU  
 E11 24 DRUILHET R/AU  
 E12 64 DRUILHET R E/AU

=> s el-e3

L2 939 ("DRUILHE P"/AU OR "DRUILHE P \*"/AU OR "DRUILHE PIERRE"/AU)

=> s l1 or l2

L3 986 L1 OR L2

=> s l3 and (hepatic or liver stage)

L4 147 L3 AND (HEPATIC OR LIVER STAGE)

=> s l4 and (T epitope or B epitope)

L5 1 L4 AND (T EPITOPE OR B EPITOPE)

=> d bib ab

L5 ANSWER 1 OF 1 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 1992-299985 [36] WPIDS

CR 1988-235148 [33]

DNN N1992-229719 DNC C1992-133808

TI Polypeptide(s) derived from **liver stage** of PLASMODIUM  
 FALCIPARUM - for vaccination against, treatment of and diagnosis of  
 malaria.

DC B04 D16 S03

IN **DRUILHE, P; GUERIN-MARCHAND, C; GUERINMARCHAND, C**

PA (INSP) INST PASTEUR; (DRUI-I) DRUILHE P; (GUER-I) GUERIN-MARCHAND C

CYC 18

PI WO 9213884 A1 19920820 (199236)\* FR 81p  
 RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE  
 W: CA JP US

FR 2672290 A1 19920807 (199240) 5p

EP 570489 A1 19931124 (199347) FR  
 R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE

EP 570489 B1 19990506 (199922) FR  
 R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE

DE 69229107 E 19990610 (199929)

ES 2133316 T3 19990916 (199946)

US 6270771 B1 20010807 (200147)

US 6319502 B1 20011120 (200174)

US 2002041882 A1 20020411 (200227)

US 2003064075 A1 20030403 (200325)

ADT WO 9213884 A1 WO 1992-FR104 19920205; FR 2672290 A1 FR 1991-1286 19910205;  
 EP 570489 A1 EP 1992-905897 19920205, WO 1992-FR104 19920205; EP 570489 B1  
 EP 1992-905897 19920205, WO 1992-FR104 19920205; DE 69229107 E DE  
 1992-629107 19920205, EP 1992-905897 19920205, WO 1992-FR104 19920205; ES  
 2133316 T3 EP 1992-905897 19920205; US 6270771 B1 Div ex US 1988-275139  
 19881006, WO 1992-FR104 19920205, US 1993-98327 19931124, Div ex US  
 1995-462062 19950605, CIP of US 1996-760000 19961203; US 6319502 B1 Div ex  
 US 1993-98327 19931124, US 1995-462625 19950605; US 2002041882 A1 Div ex  
 US 1995-462625 19950605, US 2001-837344 20010419; US 2003064075 A1 Div ex  
 WO 1992-FR104 19920205, Div ex US 1993-98327 19931124, US 2001-900963  
 20010710

FDT EP 570489 A1 Based on WO 9213884; EP 570489 B1 Based on WO 9213884; DE  
 69229107 E Based on EP 570489, Based on WO 9213884; ES 2133316 T3 Based on  
 EP 570489; US 6270771 B1 Div ex US 5599542, Div ex US 5602031, CIP of US  
 5928901, Based on WO 9213884; US 2003064075 A1 Div ex US 6270771

PRAI FR 1991-1286 19910205; FR 1987-1543 19870209

AB WO 9213884 A UPAB: 20030416

New cpd. (I) or a polypeptide compsn. includes in its structure one or  
 more peptide sequences including all or part of at least one T

**epitope** (and opt. other, esp. B, epitopes) which are characteristic of proteins produced by infectious activity of *Plasmodium falciparum* in liver cells.

More specifically, (I) corresponds to at least part of the **liver stage** specific antigen (LSA) gene (the specification includes sequences for the 3'-(1496bp) and 5'- ends (956bp) of this gene, together with the derived amino acid sequence).

USE/ADVANTAGE - (I) and Ab are useful in immunological diagnosis of malaria caused by *P. falciparum*, esp. by testing serum samples. They provide a more sensitive test than known methods. (I) can also be used in vaccines while Ab can be used therapeutically. Fragments of the nucleotide sequence can also be used diagnostically (as probe  
Dwg.0/10

=> d his

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FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS, LIFESCI, CAPLUS' ENTERED AT 07:15:32 ON 29 SEP 2003

E GUERIN MARCHAND CLAUDINE/AU

L1 86 S E1-E4  
E DRUILHE PIERRE/AU  
L2 939 S E1-E3  
L3 986 S L1 OR L2  
L4 147 S L3 AND (HEPATIC OR LIVER STAGE)  
L5 1 S L4 AND (T EPITOPE OR B EPITOPE)

=> s l4 and vaccin

L6 1 L4 AND VACCIN

=> s l4 and epitope

L7 19 L4 AND EPITOPE

=> dup rem l7

PROCESSING COMPLETED FOR L7

L8 9 DUP REM L7 (10 DUPLICATES REMOVED)

=> d bib ab 1-9

L8 ANSWER 1 OF 9 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.  
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AN 2003127917 EMBASE

TI Analysis of intra-**hepatic** peptide-specific cell recruitment in mice immunised with *Plasmodium falciparum* antigens.

AU Hebert A.; Sauzet J.-P.; Lebastard M.; Ungeheuer M.-N.; Ave P.; Huerre M.;  
**Druilhe P.**

CS P. Druilhe, U. de Parasitologie Medicale, Institut Pasteur, 25 and 28 Rue du Docteur Roux, 75724 Paris Cedex 15, France. druilhe@pasteur.fr

SO Journal of Immunological Methods, (1 Apr 2003) 275/1-2 (123-132).

Refs: 19

ISSN: 0022-1759 CODEN: JIMMBG

CY Netherlands

DT Journal; Article

FS 004 Microbiology

026 Immunology, Serology and Transplantation

LA English

SL English

AB The **liver stage** of *Plasmodium* spp. now appears as a relevant target of immune effectors triggered by the so-called "anti-sporozoite" vaccine. Since the monitoring of immune responses at the systemic level may not faithfully reflect the local protective mechanisms,

the aim of the present work was to set up a model to study the local intra-hepatic cellular responses and to compare these with the peripheral immune responses. This was achieved by intra-portal delivery of epitopic peptides, i.e. peptides containing B and T cell epitopes, which were coated onto the surface of polystyrene microbeads. The peptide-coated beads presumably mimic the hepatic schizont, and when distinct peptides are administered separately, this method of delivery allows us to decipher the immune responses resulting in mice immunised with recombinant proteins spanning several such epitopes. Using the *P. falciparum* liver stage antigen-3 (LSA3) molecule, which can induce protection against a sporozoite challenge, our results show that 25-µm microbeads could easily access the liver parenchyma by intra-portal injection and were distributed evenly in the liver. Also, LSA3-derived synthetic peptides coated onto microbeads initiated specific cell recruitment within 6 h. Depending on the LSA3 peptide used, the infiltrates induced differed in size, with the strongest cell recruitment obtained using nonrepeat II peptide (NR2)-coated microbeads with a mean leukocyte number of 79 per granuloma. Immunohistological studies of liver sections revealed that, irrespective of the delivered peptide, cells infiltrating the liver towards microbeads were mainly CD3(+) T lymphocytes, both CD4(+) (70 to 80%) and CD8(+) (20 to 30%) subtypes, macrophages and dendritic cells. Cells infiltrating the granuloma had features of activated cells, with evidence of VLA-4 cell-surface expression, and production of IFN-γ and IL-4. Analysis of the peripheral B and T-cell responses in the same animals revealed that, whereas the local responses were directed mainly towards NR2 and repeat peptides (RE), the peripheral T-cell response to these peptides was weak and infrequent, although antibody production was high. .COPYRGHT. 2003 Elsevier Science B.V. All rights reserved.

L8 ANSWER 2 OF 9 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN  
AN 2003-129263 [12] WPIDS  
DNC C2003-033056  
TI New polynucleotide from Plasmodium falciparum and derived protein, useful as immunogen for antimalarial vaccines and for preparing diagnostic or therapeutic antibodies.  
DC B04 D16  
IN DRUILHE, P; GRUNER, A; GRUNER, A C; GRUENER, A  
PA (INSP) INST PASTEUR  
CYC 100  
PI WO 2002092628 A2 20021121 (200312)\* FR 115p  
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
NL OA PT SD SE SL SZ TR TZ UG ZM ZW  
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT  
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM  
ZW  
CA 2345206 A1 20021116 (200312) FR  
CA 2346968 A1 20021123 (200312) FR  
CA 2382977 A1 20021116 (200312) FR  
ADT WO 2002092628 A2 WO 2002-FR1637 20020515; CA 2345206 A1 CA 2001-2345206  
20010516; CA 2346968 A1 CA 2001-2346968 20010523; CA 2382977 A1 CA  
2002-2382977 20020515  
PRAI CA 2001-2346968 20010523; CA 2001-2345206 20010516  
AB WO 200292628 A UPAB: 20030218  
NOVELTY - Isolated or purified polynucleotide (I), comprising at least 60,  
preferably 95, % identity with a 192 (DG747; S1) or 351 (DG772; S2), base  
pair sequence, given in the specification, is new.  
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the  
following:  
(1) isolated or purified nucleic acid (Ia) comprising at least 10  
consecutive nucleotides (nt) from (S1) or (S2);

(2) isolated or purified nucleic acid (Ib) that hybridizes under highly stringent conditions to (S1) or (S2);  
 (3) isolated or purified polypeptide (II) that is:  
 (a) encoded by (I)-(Ib);  
 (b) at least 60, preferably 95,% homologous with a 64 (S3) or 117 (S4) residue amino acid sequence, given in the specification;  
 (c) at least 40, preferably 85,% identical with any of the sequences of (b);  
 (4) recombinant or chimeric polypeptides (IIa) containing at least one (II);  
 (5) isolated or purified antigen (Ag) comprising (I)-(Ib), (II) or (IIa);  
 (6) antigenic conjugate (C) comprising Ag adsorbed on a carrier;  
 (7) mono- or poly-clonal antibodies (Ab) that react specifically with at least one Ag and/or (C);  
 (8) cloning or expression vector containing (I)-(Ib);  
 (9) host cells containing the vector of (8);  
 (10) immunogenic composition, or antimalaria vaccine, containing Ag or (C);  
 (11) composition containing Ab;  
 in vitro diagnosis of malaria caused by Plasmodium falciparum, using Ab, Ag or (C); and  
 (12) kit for process of (12).

ACTIVITY - Protozoacide.

MECHANISM OF ACTION - Vaccine; induction of interferon gamma production by leukocytes.

The plasmid pNAK747 (expressing DG747) was injected intramuscularly into BALB/c mice (four times). When challenged with irradiated P. falciparum sporozoites, lymphocyte proliferation (index of stimulation 23.6 and 33.7) occurred in two of three animals, and all three showed induction of interferon gamma (15-40 international units/ml).

USE - (I), also their fragments and complements, and polypeptides (II) encoded by them, are useful as immunogens/vaccines for protection against infection by Plasmodium falciparum. They, and their conjugates and antibodies (Ab) raised against (II), are useful in treating P. falciparum malaria and for in vitro diagnosis of infection.  
 Dwg.0/3

L8 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2001:578081 CAPLUS

DN 135:166008

TI Protein sequence of plasmodium falciparum liver stage antigen LSA and its use in diagnosis and therapeutics for malaria

IN **Guerin-Marchand, Claudine; Druilhe, Pierre**

PA Institut Pasteur, Fr.

SO U.S., 57 pp., Cont.-in-part of U.S. 5,928,901.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6270771	B1	20010807	US 1993-98327	19931124
	US 5599542	A	19970204	US 1988-275139	19881006
	FR 2672290	A1	19920807	FR 1991-1286	19910205
	FR 2672290	B1	19950421		
	WO 9213884	A1	19920820	WO 1992-FR104	19920205
	W: CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
	US 5589343	A	19961231	US 1995-463512	19950605
	US 5602031	A	19970211	US 1995-462062	19950605
	US 6319502	B1	20011120	US 1995-462625	19950605
	US 5928901	A	19990727	US 1996-760000	19961203

US 2003064075 A1 20030403 US 2001-900963 20010710  
PRAI US 1988-275139 A3 19881006  
FR 1991-1286 A 19910205  
WO 1992-FR104 W 19920205  
US 1995-462062 A3 19950605  
US 1996-760000 A2 19961203  
FR 1987-1543 A 19870209  
WO 1988-FR74 W 19880209  
US 1993-98327 A3 19931124

AB The invention discloses a mol. or polypeptide compn. characterized by the presence in its structure of one or more peptide sequences bearing all or part of one or more T epitopes, and possibly other epitopes, particularly B epitopes, characteristic of proteins resulting from the infectious activity of *P. falciparum* **hepatic** cells. Also disclosed is the use of these mols. in tests, and a kit for in vitro diagnosis of paludism from a biol. sample from the individual in whom the disease is to be detected.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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AN 2001195101 EMBASE

TI Human antibodies against *Plasmodium falciparum* **liver-stage** antigen 3 cross-react with *Plasmodium yoelii* preerythrocytic-stage epitopes and inhibit sporozoite invasion in vitro and in vivo.

AU Brahimi K.; Badell E.; Sauzet J.-P.; BenMohamed L.; Daubersies P.; Guerin-Marchand C.; Snounou G.; Druilhe P.

CS P. Druilhe, Bio-Medical Parasitology Unit, Institut Pasteur, 28, rue du Docteur Roux, 75015 Paris, France. druilhe@pasteur.fr

SO Infection and Immunity, (2001) 69/6 (3845-3852).  
Refs: 33  
ISSN: 0019-9567 CODEN: INFIBR

CY United States

DT Journal; Article

FS 004 Microbiology  
026 Immunology, Serology and Transplantation

LA English

SL English

AB The *Plasmodium falciparum* **liver-stage** antigen 3 (LSA3), a recently identified preerythrocytic antigen, induces protection against malaria in chimpanzees. Using antibodies from individuals with hyperimmunity to malaria affinity purified on recombinant or synthetic polypeptides of LSA3, we identified four non-cross-reactive B-cell epitopes in *Plasmodium yoelii* preerythrocytic stages. On sporozoites the *P. yoelii* protein detected has a molecular mass similar to that of LSA3. T-cell epitopes cross-reacting with *P. yoelii* were also demonstrated using peripheral blood lymphocytes from LSA3-immunized chimpanzees. In contrast, no cross-reactive epitopes were found in *Plasmodium berghei*. LSA3-specific human antibodies exerted up to 100% inhibition of in vitro invasion of *P. yoelii* sporozoites into mouse hepatocytes. This strong in vitro activity was reproduced in vivo by passive transfer of LSA3 antibodies. These results indicate that the homologous epitopes may be biologically functional and suggest that *P. yoelii* could be used as a model to assess the antiparasitic activity of anti-LSA3 antibodies.

L8 ANSWER 5 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
DUPLICATE 1

AN 2001:379920 BIOSIS

DN PREV200100379920

TI Long synthetic peptides encompassing the *Plasmodium falciparum* LSA3 are the target of human B and T cells and are potent inducers of B helper, T

helper and cytolytic T cell responses in mice.

AU Perlaza, Blanca Liliana; Sauzet, Jean-Pierre; Balde, Aissatou Toure; Brahim, Karima; Tall, Adama; Corradin, Giampietro (1); **Druihe, Pierre**

CS (1) Institut de Biochimie, Chemin des Boveresses, Epalinges, CH-1000, Lausanne: Giampietro.Corradin@ib.unil.ch, druilhe@pasteur.fr Switzerland

SO European Journal of Immunology, (July, 2001) Vol. 31, No. 7, pp. 2200-2209. print.  
ISSN: 0014-2980.

DT Article

LA English

SL English

AB We synthesized 17 long synthetic peptides (LSP) spanning the whole 200-kDa Plasmodium falciparum **liver stage** antigen-3 (LSA3), an antigen that induces protection in chimpanzee, and analyzed their immunogenicity in BALB/c mice and their antigenicity in individuals living in a hyper-endemic malaria area. Our findings show that both specific antibodies and T cell proliferation against most LSA3-LSP develop in malaria-exposed adults. All individuals studied had detectable antibodies against a minimum of 6 and a maximum of 15 polypeptides. It is noteworthy that antibody prevalence and titers were as high against non-repeat as repeat regions. Although the extent of T cell reactivity was lower than that observed for B cells, most of the sequences contained at least one T helper **epitope**, indicating that the majority of LSA3-LSP contain both B and T cell epitopes within the same sequence. Injection of LSA3-LSP with SBSA2 adjuvant in mice, showed strong immunogenicity for most of them, eliciting both T cell responses and specific antibody production. While all the peptides were immunogenic for B cells, different patterns of T cell responses were induced. These peptides were thus classified in three sets according to the levels of the T cell proliferative and of the IFN-gamma-specific responses. Importantly, antibodies and T cells against some of the LSP were able to recognize LSA3 native protein on P. falciparum sporozoites. Additionally, some LSP (44-119, 1026-1095, 1601-1712) also contained epitopes recognized by H-2d class I-restricted T cells. These results led to the identification of numerous domains that are highly antigenic and immunogenic within the LSA3 protein, and underline the value of the LSP approach for vaccine development.

L8 ANSWER 6 OF 9 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 2

AN 1992-299985 [36] WPIDS

CR 1988-235148 [33]

DNN N1992-229719 DNC C1992-133808

TI Polypeptide(s) derived from **liver stage** of PLASMODIUM FALCIPARUM - for vaccination against, treatment of and diagnosis of malaria.

DC B04 D16 S03

IN **DRUILHE, P**; **GUERIN-MARCHAND, C**; GUERINMARCHAND, C

PA (INSP) INST PASTEUR; (DRUI-I) **DRUILHE P**; (GUER-I) GUERIN-MARCHAND C

CYC 18

PI WO 9213884 A1 19920820 (199236)\* FR 81p  
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE  
W: CA JP US

FR 2672290 A1 19920807 (199240) 5p

EP 570489 A1 19931124 (199347) FR

R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE

EP 570489 B1 19990506 (199922) FR

R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE

DE 69229107 E 19990610 (199929)

ES 2133316 T3 19990916 (199946)

US 6270771 B1 20010807 (200147)

US 6319502 B1 20011120 (200174)

US 2002041882 A1 20020411 (200227)

US 2003064075 A1 20030403 (200325)

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on STN  
AN 2003127917 EMBASE  
TI Analysis of intra-hepatic peptide-specific cell recruitment in  
mice immunised with Plasmodium falciparum antigens.  
AU Hebert A.; Sauzet J.-P.; Lebastard M.; Ungeheuer M.-N.; Ave P.; Huerre M.;  
Druilhe P.  
CS P. Druilhe, U. de Parasitologie Medicale, Institut Pasteur, 25 and 28 Rue  
du Docteur Roux, 75724 Paris Cedex 15, France. druilhe@pasteur.fr  
SO Journal of Immunological Methods, (1 Apr 2003) 275/1-2 (123-132).  
Refs: 19  
ISSN: 0022-1759 CODEN: JIMMBG  
CY Netherlands  
DT Journal; Article  
FS 004 Microbiology  
026 Immunology, Serology and Transplantation  
LA English  
SL English

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FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS,  
LIFESCI, CAPLUS' ENTERED AT 07:15:32 ON 29 SEP 2003

E GUERIN MARCHAND CLAUDINE/AU

L1 86 S E1-E4  
E DRUILHE PIERRE/AU  
L2 939 S E1-E3  
L3 986 S L1 OR L2  
L4 147 S L3 AND (HEPATIC OR LIVER STAGE)  
L5 1 S L4 AND (T EPITOPE OR B EPITOPE)  
L6 1 S L4 AND VACCIN  
L7 19 S L4 AND EPITOPE  
L8 9 DUP REM L7 (10 DUPLICATES REMOVED)

=> s l4 and epitope

L9 19 L4 AND EPITOPE

=> dup rem l4

PROCESSING COMPLETED FOR L4

L10 54 DUP REM L4 (93 DUPLICATES REMOVED)

=> s l10 and (vaccin or antigenic or immunogen)

OR IS NOT A RECOGNIZED COMMAND

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For a list of commands available to you in the current file, enter

"HELP COMMANDS" at an arrow prompt (=>).

=> .

. IS NOT A RECOGNIZED COMMAND

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For a list of commands available to you in the current file, enter

"HELP COMMANDS" at an arrow prompt (=>).

=> s l10 and (vaccin or antigenic or immunogen)

L11 14 L10 AND (VACCIN OR ANTIGENIC OR IMMUNOGEN)

=> d bib ab 1-14

L11 ANSWER 1 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
 AN 2003:141875 BIOSIS  
 DN PREV200300141875  
 TI Pre-erythrocytic antigens of Plasmodium falciparum: From rags to riches.  
 AU Gruner, Anne Charlotte; Snounou, Georges; Brahimi, Karima; Letourneur,  
 Franck; Renia, Laurent; **Druilhe, Pierre (1)**  
 CS (1) Unite de Parasitologie Biomedicale, Institut Pasteur, 25 Rue du Dr  
 Roux, 75724, Paris Cedex 15, France: druilhe@pasteur.fr France  
 SO Trends in Parasitology, (February 2003, 2003) Vol. 19, No. 2, pp. 74-78.  
 print.  
 ISSN: 1471-4922.  
 DT Article  
 LA English  
 AB A growing number of Plasmodium genomes have joined the sequencing  
 treadmill, and the genome of Plasmodium falciparum has recently been  
 published. Most malaria vaccinologists will soon be confronted by a  
 bewildering array of new potential antigens from the recently completed  
 genome of this parasite. However, for those aiming to target the  
 pre-erythrocytic stages of the **hepatic** parasite, the wait might  
 be long. In the absence of readily available materials and specific  
 reagents, the selection of pre-erythrocytic antigens from raw sequence  
 data is likely to prove difficult. Here, current knowledge of  
 pre-erythrocytic antigens is updated in the light of recent results, and  
 the post-genomic prospects of completing the **antigenic**  
 repertoire of these immunologically important and intriguing stages is  
 discussed.

L11 ANSWER 2 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
 AN 2001:379920 BIOSIS  
 DN PREV200100379920  
 TI Long synthetic peptides encompassing the Plasmodium falciparum LSA3 are  
 the target of human B and T cells and are potent inducers of B helper, T  
 helper and cytolytic T cell responses in mice.  
 AU Perlaza, Blanca Liliana; Sauzet, Jean-Pierre; Balde, Aissatou Toure;  
 Brahimi, Karima; Tall, Adama; Corradin, Giampietro (1); **Druilhe,  
 Pierre**  
 CS (1) Institut des Biochimie, Chemin des Boveresses, Epalinges, CH-1000,  
 Lausanne: Giampietro.Corradin@ib.unil.ch, druilhe@pasteur.fr Switzerland  
 SO European Journal of Immunology, (July, 2001) Vol. 31, No. 7, pp.  
 2200-2209. print.  
 ISSN: 0014-2980.  
 DT Article  
 LA English  
 SL English  
 AB We synthesized 17 long synthetic peptides (LSP) spanning the whole 200-kDa  
 Plasmodium falciparum **liver stage** antigen-3 (LSA3), an  
 antigen that induces protection in chimpanzee, and analyzed their  
 immunogenicity in BALB/c mice and their antigenicity in individuals living  
 in a hyper-endemic malaria area. Our findings show that both specific  
 antibodies and T cell proliferation against most LSA3-LSP develop in  
 malaria-exposed adults. All individuals studied had detectable antibodies  
 against a minimum of 6 and a maximum of 15 polypeptides. It is noteworthy  
 that antibody prevalence and titers were as high against non-repeat as  
 repeat regions. Although the extent of T cell reactivity was lower than  
 that observed for B cells, most of the sequences contained at least one T  
 helper epitope, indicating that the majority of LSA3-LSP contain both B  
 and T cell epitopes within the same sequence. Injection of LSA3-LSP with  
 SBSA2 adjuvant in mice, showed strong immunogenicity for most of them,  
 eliciting both T cell responses and specific antibody production. While  
 all the peptides were immunogenic for B cells, different patterns of T  
 cell responses were induced. These peptides were thus classified in three  
 sets according to the levels of the T cell proliferative and of the

IFN-gamma-specific responses. Importantly, antibodies and T cells against some of the LSP were able to recognize LSA3 native protein on *P. falciparum* sporozoites. Additionally, some LSP (44-119, 1026-1095, 1601-1712) also contained epitopes recognized by H-2d class I-restricted T cells. These results led to the identification of numerous domains that are highly **antigenic** and immunogenic within the LSA3 protein, and underline the value of the LSP approach for vaccine development.

- L11 ANSWER 3 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
 AN 2001:32859 BIOSIS  
 DN PREV200100032859  
 TI Protection against *Plasmodium falciparum* malaria in chimpanzees by immunization with the conserved pre-erythrocytic **liver-stage** antigen 3.  
 AU Daubersies, Pierre (1); Thomas, Alan W.; Millet, Pascal; Brahimi, Karima; Langermans, Jan A. M.; Ollomo, Benjamin; Mohamed, Lbachir Ben; Slierendregt, Bas; Eling, Wijnand; Van Belkum, Alex; Dubreuil, Guy; Meis, Jacques F. G. M.; **Guerin-Marchand, Claudine**; Cayphas, Sylvie; Cohen, Joe; Gras-Masse, Helene; **Druilhe, Pierre**  
 CS (1) Unite de Parasitologie Biomedicale, Institut Pasteur, 28 rue du Dr Roux, 75015, Paris: druilhe@pasteur.fr France  
 SO Nature Medicine, (November, 2000) Vol. 6, No. 11, pp. 1258-1263. print. ISSN: 1078-8956.  
 DT Article  
 LA English  
 SL English  
 AB In humans, sterile immunity against malaria can be consistently induced through exposure to the bites of thousands of irradiated infected mosquitoes. The same level of protection has yet to be achieved using subunit vaccines. Recent studies have indicated an essential function for intra-**hepatic** parasites, the stage after the mosquito bite, and thus for antigens expressed during this stage. We report here the identification of **liver-stage** antigen 3, which is expressed both in the mosquito and **liver-stage** parasites. This *Plasmodium falciparum* 200-kilodalton protein is highly conserved, and showed promising **antigenic** and immunogenic properties. In chimpanzees (*Pan troglodytes*), the primates most closely related to humans and that share a similar susceptibility to *P. falciparum* **liver-stage** infection, immunization with LSA-3 induced protection against successive heterologous challenges with large numbers of *P. falciparum* sporozoites.
- L11 ANSWER 4 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
 AN 1996:287901 BIOSIS  
 DN PREV199699010257  
 TI Immunity to *Plasmodium berghei* exoerythrocytic forms derived from irradiated sporozoites.  
 AU Chatterjee, Shyama (1); Francois, G.; **Druilhe, P.**; Timperman, G.; Wery, M.  
 CS (1) Dep. Protozoology, Institut Tropical Med., Nationalstraat 155, Antwerp, B-2000 Belgium  
 SO Parasitology Research, (1996) Vol. 82, No. 4, pp. 297-303. ISSN: 0932-0113.  
 DT Article  
 LA English  
 AB The nature of immunity generated by *Plasmodium berghei* exoerythrocytic (EE) stages developing from irradiated sporozoites was studied using in vivo parameters of host protection on immunization with irradiated sporozoites and in vitro parameters of inhibition of sporozoite invasion and EE form development by serum antibodies from immunized mice. On in vivo challenge of immunized mice by sporozoites, protection was observed in an irradiation-dose-dependent manner. This finding stresses that protection is dependent on the irradiation dose of sporozoites that allows

sporozoite penetration yet controls EE form development within the liver. Using the human hepatoma line Hep G2 as host cells in vitro, we observed that serum antibodies raised in mice immunized with irradiated sporozoites reacted with sporozoite- and **hepatic-stage** parasites in an immunofluorescent antibody test (IFAT). No reactivity was observed with blood-stage parasites. Serum antibodies from mice immunized with 6- to 18-krad-irradiated sporozoites inhibited sporozoite invasion and caused severe inhibition of EE form development in hepatoma cells, pointing to the **antigenic** content of EE forms developing from irradiated sporozoites (irra EE forms) as critical immunogens. Moreover, in an enzyme-linked immunosorbent assay (ELISA), serum antibodies raised to 12-krad-irradiated sporozoites showed reactivity to synthetic peptides representing the conserved Region II sequences of the *P. falciparum* circumsporozoite (CS) protein as well as the *P. falciparum* **liver-stage-specific** antigen (LSA-1)-based repeat sequences, thus implicating an important role for both the sporozoite and the **hepatic** stage in protection.

- L11 ANSWER 5 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
 AN 1996:268749 BIOSIS  
 DN PREV199698824878  
 TI A novel *Plasmodium falciparum* sporozoite and **liver stage** antigen (SALSA) defines major B, T helper, and CTL epitopes.  
 AU Bottius, Emmanuel; Benmohamed, Lbahir; Brahimi, Karima; Gras, Helene; Lepers, Jean-Paul; Raharimalala, Lucie; Aikawa, Masamichi; Meis, Jacques; Slierendregt, Bas; Tartar, Andre; Thomas, Alan; **Druilhe, Pierre**  
 (1)  
 CS (1) Laboratoire de Parasitologie Bio-Medicale, Inst. Pasteur, 28 rue du Dr. Roux, 75724 Paris Cedex 15 France  
 SO Journal of Immunology, (1996) Vol. 156, No. 8, pp. 2876-2884.  
 ISSN: 0022-1767.  
 DT Article  
 LA English  
 AB In the search for subunit vaccines that are able to induce the type of sterile, protective immunity achieved by irradiated sporozoites, there is increasing evidence that defense mechanisms directed at the intrahepatic stage and Ags expressed at this stage are critical. We have initiated a systematic search for such molecules and report here the identification and partial characterization of a novel *Plasmodium falciparum* gene encoding a 70-kDa protein, expressed in both sporozoite and liver stages (SALSA), with a vaccine potential that stems from its **antigenic** features. Antigenicity and immunogenicity studies were conducted in individuals exposed to malaria, in immunized mice, and in chimpanzees, using a recombinant protein and two synthetic peptides. Results show that the SALSA nonrepetitive sequence defines 1) major B cell epitopes, as shown by a high prevalence of Abs to each peptide in three African areas differing in their level of endemicity; 2) Th epitopes, as demonstrated by lymphoproliferation and IFN-gamma secretion in cells from the individuals from one of the low transmission areas, as well as helper effect upon Ab secretion in mice; and 3) epitopes for cytolytic lymphocytes, demonstrated in immunized and sporozoite-challenged chimpanzees, and associated with MHC class I leukocyte Ags. The latter are of particular importance, because this is the only part of the malaria life cycle in which the parasite is located in a cell expressing class I Ags and because CD8+ lymphocytes were found to be responsible for protection in experimental models.
- L11 ANSWER 6 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
 AN 1995:257419 BIOSIS  
 DN PREV199598271719  
 TI Identification of conserved **antigenic** components for a cytotoxic T lymphocyte-inducing vaccine against malaria.  
 AU Aidoo, M.; Lalvani, A.; Allsopp, C. E. M.; Plebanski, M.; Meisner, S. J.; Krausa, P.; Browning, M.; Morris-Jones, S.; Gotch, F.; Fidock, D. A.;

Takiguchi, M.; Robson, K. J. H.; Greenwood, B. M.; **Druilhe, P.**;  
Whittle, H. C.; Hill, A. S. S. (1)

CS (1) Inst. Mol. Med., John Radcliffe Hosp., Oxford OX3 9DU UK  
SO Lancet (North American Edition), (1995) Vol. 345, No. 8956, pp. 1003-1007.  
ISSN: 0099-5355.

DT Article

LA English

AB Several cellular and humoral mechanisms probably play a role in natural immunity to Plasmodium falciparum malaria, but the development of an effective vaccine has been impeded by uncertainty as to which antigens are targeted by protective immune responses. Experimental models of malaria have shown that cytotoxic T lymphocytes (CTL) which kill parasite-infected hepatocytes can provide complete protective immunity against certain species of Plasmodium in mice, and studies in The Gambia have provided indirect evidence that CTL play a protective role against P. falciparum in humans. By using an HLA-based approach, termed reverse immunogenetics, we have previously identified peptide epitopes for CTL in **liver-stage** antigen-1 and the circumsporozoite protein of P. falciparum. We have extended this work to identify CTL epitopes for HLA class I antigens that are found in most individuals from Caucasian and African populations. Most of these epitopes are in conserved regions of P. falciparum. CTL peptide epitopes were found in a further two antigens, thrombospondin-related anonymous protein and sporozoite threonine and asparagine rich protein, indicating that a subunit vaccine designed to induce a protective CTL response may need to include parts of several parasite antigens. However, CTL levels in both children with malaria and in semi-immune adults from an endemic area were low suggesting that boosting these low levels by immunisation might provide substantial or even complete protection against infection and disease.

L11 ANSWER 7 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
AN 1992:166739 BIOSIS  
DN BA93:89064

TI **ANTIGENIC ANALYSIS OF PLASMODIUM-YOELII LIVER STAGES BY FLUORESCENCE ANTIBODY ASSAYS.**

AU LONDONO J A; SEDEGAH M; CHAROENVIT Y; BEAUDOIN R L; **DRUILHE P**  
CS MEDICAL PARASITOL., 28 RUE DU DOCTEUR ROUX, 75724 PARIS CEDEX 15, FRANCE.  
SO TROP MED PARASITOL., (1991) 42 (4), 381-385.  
CODEN: TMPAEY. ISSN: 0177-2392.

FS BA; OLD

LA English

AB Little is known about the immune response against **liver stage** antigens which were first described for Plasmodium falciparum. In order to provide a basis for experimental studies, we analyzed antigenically the liver stages of Plasmodium yoelii using sera of restricted specificity. Several distinct fluorescence patterns could be described in maturing liver forms. One pattern was identified as corresponding to antigens specific to the liver phase which are also species specific. Another pattern corresponds to sporozoite surface antigens which were predominant in liver trophozoites. Trophozoite-like liver forms were detected at least 7 days after the injection of irradiated sporozoites suggesting that parasites may persist and contribute to the community induced by this procedure.

L11 ANSWER 8 OF 14 MEDLINE on STN

AN 96183242 MEDLINE

DN 96183242 PubMed ID: 8609407

TI A novel Plasmodium falciparum sporozoite and **liver stage** antigen (SALSA) defines major B, T helper, and CTL epitopes.

AU Bottius E; BenMohamed L; Brahimi K; Gras H; Lepers J P; Raharimalala L; Aikawa M; Meis J; Slierendregt B; Tartar A; Thomas A; **Druilhe P**  
CS Biomedical Parasitology, Pasteur Institute, Paris, France.  
SO JOURNAL OF IMMUNOLOGY, (1996 Apr 15) 156 (8) 2874-84.

AB A brief account is given of the 6 approaches being followed in the development of vaccines against malaria: anti-sporozoite; anti-liver stage; anti-erythrocytic stages; anti-disease; altruistic (anti-sexual stage); attenuated strains.

L11 ANSWER 12 OF 14 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN  
AN 2003-129263 [12] WPIDS  
DNC C2003-033056  
TI New polynucleotide from Plasmodium falciparum and derived protein, useful as **immunogen** for antimalarial vaccines and for preparing diagnostic or therapeutic antibodies.  
DC B04 D16  
IN **DRUILHE, P**; GRUNER, A; GRUNER, A C; GRUENER, A  
PA (INSP) INST PASTEUR  
CYC 100  
PI WO 2002092628 A2 20021121 (200312)\* FR 115p  
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
NL OA PT SD SE SL SZ TR TZ UG ZM ZW  
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT  
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM  
ZW  
CA 2345206 A1 20021116 (200312) FR  
CA 2346968 A1 20021123 (200312) FR  
CA 2382977 A1 20021116 (200312) FR  
ADT WO 2002092628 A2 WO 2002-FR1637 20020515; CA 2345206 A1 CA 2001-2345206  
20010516; CA 2346968 A1 CA 2001-2346968 20010523; CA 2382977 A1 CA  
2002-2382977 20020515  
PRAI CA 2001-2346968 20010523; CA 2001-2345206 20010516  
AB WO 200292628 A UPAB: 20030218  
NOVELTY - Isolated or purified polynucleotide (I), comprising at least 60,  
preferably 95,% identity with a 192 (DG747; S1) or 351 (DG772; S2), base  
pair sequence, given in the specification, is new.  
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the  
following:  
(1) isolated or purified nucleic acid (Ia) comprising at least 10  
consecutive nucleotides (nt) from (S1) or (S2);  
(2) isolated or purified nucleic acid (Ib) that hybridizes under  
highly stringent conditions to (S1) or (S2);  
(3) isolated or purified polypeptide (II) that is:  
(a) encoded by (I)-(Ib);  
(b) at least 60, preferably 95,% homologous with a 64 (S3) or 117  
(S4) residue amino acid sequence, given in the specification;  
(c) at least 40, preferably 85,% identical with any of the sequences  
of (b);  
(4) recombinant or chimeric polypeptides (IIa) containing at least  
one (II);  
(5) isolated or purified antigen (Ag) comprising (I)-(Ib), (II) or  
(IIa);  
(6) **antigenic** conjugate (C) comprising Ag adsorbed on a  
carrier;  
(7) mono- or poly-clonal antibodies (Ab) that react specifically with  
at least one Ag and/or (C);  
(8) cloning or expression vector containing (I)-(Ib);  
(9) host cells containing the vector of (8);  
(10) immunogenic composition, or antimalaria vaccine, containing Ag  
or (C);  
(11) composition containing Ab;  
in vitro diagnosis of malaria caused by Plasmodium falciparum, using  
Ab, Ag or (C); and  
(12) kit for process of (12).  
ACTIVITY - Protozoacide.

MECHANISM OF ACTION - Vaccine; induction of interferon gamma production by leukocytes.

The plasmid pNAK747 (expressing DG747) was injected intramuscularly into BALB/c mice (four times). When challenged with irradiated *P. falciparum* sporozoites, lymphocyte proliferation (index of stimulation 23.6 and 33.7) occurred in two of three animals, and all three showed induction of interferon gamma (15-40 international units/ml).

USE - (I), also their fragments and complements, and polypeptides (II) encoded by them, are useful as immunogens/vaccines for protection against infection by *Plasmodium falciparum*. They, and their conjugates and antibodies (Ab) raised against (II), are useful in treating *P. falciparum* malaria and for in vitro diagnosis of infection.

Dwg.0/3

L11 ANSWER 13 OF 14 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN  
AN 2002-373883 [41] WPIDS  
DNC C2002-105903  
TI Vaccine for treatment or prevention of malaria, comprises **liver stage** antigen and adjuvant that induces Th1 response.  
DC B04 D16  
IN COHEN, J; DRUILHE, P  
PA (INSP) INST PASTEUR; (SMIK) SMITHKLINE BEECHAM BIOLOGICALS; (GLAX) GLAXOSMITHKLINE BIOLOGICALS SA  
CYC 98  
PI EP 1201250 A1 20020502 (200241)\* EN 56p  
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI  
WO 2002038176 A2 20020516 (200241) EN  
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW  
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW  
AU 2002029522 A 20020521 (200260)  
EP 1328292 A2 20030723 (200350) EN  
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR  
ADT EP 1201250 A1 EP 2000-203724 20001025; WO 2002038176 A2 WO 2001-EP12349 20011023; AU 2002029522 A AU 2002-29522 20011023; EP 1328292 A2 EP 2001-990374 20011023, WO 2001-EP12349 20011023  
FDT AU 2002029522 A Based on WO 2002038176; EP 1328292 A2 Based on WO 2002038176  
PRAI EP 2000-203724 20001025  
AB EP 1201250 A UPAB: 20020701  
NOVELTY - A vaccine (A) comprising a Th1-inducing adjuvant (I) and a protective **liver-stage** antigen (LSA), or its immunogenic fragment, from a human malaria parasite, where LSA is a fragment of LSA-3, then (I) is not montanide, is new.  
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for making (A) comprising admixing QS21, de-O-acylated monophosphoryl-lipid A (3D-MPL) and the oil in water emulsion with a protecting LSA of a human malaria parasite.  
ACTIVITY - Protozoacide. Chimpanzees were immunized subcutaneously with 50 micro g of a recombinant protein of LSA-3 and glutathione-S-transferase, formulated in SBAS2 adjuvant (an oil-in-water emulsion containing QS21 and de-O-acylated monophosphoryl-lipid A (3D-MPL)). Four doses were given (weeks 0, 4, 8 and 26), then the animals were challenged with *Plasmodium falciparum* sporozoites; 20000 at week 33 and 10 million at week 46. One animal was protected completely against both challenges; the other showed a delay of 1 day for patency at the lower challenge and was not protected against the higher challenge.  
MECHANISM OF ACTION - Vaccine.

## WEST Search History

DATE: Monday, September 29, 2003

<u>Set Name</u> side by side	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u> result set
<i>DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=ADJ</i>			
L10	l6 and B epitope	18	L10
L9	L6	1137	L9
L8	L7 and vaccin\$	16	L8
L7	L6 and T epitope	16	L7
L6	malaria and (hepatic or liver stage)	1137	L6
L5	L4 and (hepatic or liver stage)	7	L5
L4	L2 and malaria adj10 epitope	7	L4
L3	L2 and malaria adj10 hepatic	3	L3
L2	druilhe-pierre.in.	26	L2
L1	guerin-marchand-claudine.in.	8	L1

END OF SEARCH HISTORY

TI A **liver-stage**-specific antigen of Plasmodium  
 falciparum characterized by gene cloning;  
 peptide isolation  
 AU Guerin-Marchand C; Druilhe P; Galey B; Londono A;  
 Patarapotikul J; \*Langsley G  
 CS Inst.Pasteur  
 LO Unite de Parasitologie Experimentale, Institut Pasteur, Paris, France.  
 SO Nature; (1987) 329, 6135, 164-67  
 CODEN: NATUAS  
 DT Journal  
 LA English  
 AB A genomic expression library of Plasmodium falciparum Tak9.96 DNA clone  
 was screened with human serum of restricted specificity to the  
 pre-erythrocytic stages of development of the protozoon. 3 Clones,  
 DG145, DG199 and DG307, were obtained. Antibodies purified from the  
 original serum and selected on these clones reacted specifically with  
 liver schizonts. DG145, DG199 and DG307 were all derived from the same  
 region of the P. falciparum genome. The DNA sequence of DG307 was  
 determined and a synthetic peptide prepared. The clone contained a DNA  
 fragment of 196 bp composed entirely of a 51 bp repeat. The inferred  
 amino acid sequence comprised a 17-residue peptide rich in glutamine,  
 glutamic acid and leucine. The sequence was highly conserved. The  
 synthetic peptide reacted equally with human antibodies affinity-purified  
 on the fusion proteins of clones DG307, 145 and 199. Its reaction with  
 10 African sera indicate that a single 17-amino acid repeat carries at  
 least 1 **epitope** corresponding to an antibody specificity in  
 human sera. The role and function of this **liver-stage**  
 -specific antigen may now be studied. (17 ref)

=> d hia

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 individual files.

REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):.

L8 ANSWER 1 OF 9 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 AN 2003127917 EMBASE  
 TI Analysis of intra-**hepatic** peptide-specific cell recruitment in  
 mice immunised with Plasmodium falciparum antigens.  
 AU Hebert A.; Sauzet J.-P.; Lebastard M.; Ungeheuer M.-N.; Ave P.; Huerre M.;  
 Druilhe P.  
 CS P. Druilhe, U. de Parasitologie Medicale, Institut Pasteur, 25 and 28 Rue  
 du Docteur Roux, 75724 Paris Cedex 15, France. druilhe@pasteur.fr  
 SO Journal of Immunological Methods, (1 Apr 2003) 275/1-2 (123-132).  
 Refs: 19  
 ISSN: 0022-1759 CODEN: JIMMBG  
 CY Netherlands  
 DT Journal; Article  
 FS 004 Microbiology  
 026 Immunology, Serology and Transplantation  
 LA English  
 SL English

=> d hia

'HIA' IS NOT A VALID FORMAT

In a multifile environment, a format can only be used if it is valid  
 in at least one of the files. Refer to file specific help messages  
 or the STNGUIDE file for information on formats available in

ADT WO 9213884 A1 WO 1992-FR104 19920205; FR 2672290 A1 FR 1991-1286 19910205; EP 570489 A1 EP 1992-905897 19920205, WO 1992-FR104 19920205; EP 570489 B1 EP 1992-905897 19920205, WO 1992-FR104 19920205; DE 69229107 E DE 1992-629107 19920205, EP 1992-905897 19920205, WO 1992-FR104 19920205; ES 2133316 T3 EP 1992-905897 19920205; US 6270771 B1 Div ex US 1988-275139 19881006, WO 1992-FR104 19920205, US 1993-98327 19931124, Div ex US 1995-462062 19950605, CIP of US 1996-760000 19961203; US 6319502 B1 Div ex US 1993-98327 19931124, US 1995-462625 19950605; US 2002041882 A1 Div ex US 1995-462625 19950605, US 2001-837344 20010419; US 2003064075 A1 Div ex WO 1992-FR104 19920205, Div ex US 1993-98327 19931124, US 2001-900963 20010710

FDT EP 570489 A1 Based on WO 9213884; EP 570489 B1 Based on WO 9213884; DE 69229107 E Based on EP 570489, Based on WO 9213884; ES 2133316 T3 Based on EP 570489; US 6270771 B1 Div ex US 5599542, Div ex US 5602031, CIP of US 5928901, Based on WO 9213884; US 2003064075 A1 Div ex US 6270771

PRAI FR 1991-1286 19910205; FR 1987-1543 19870209

AB WO 9213884 A UPAB: 20030416

New cpd. (I) or a polypeptide compsn. includes in its structure one or more peptide sequences including all or part of at least one T **epitope** (and opt. other, esp. B, epitopes) which are characteristic of proteins produced by infectious activity of Plasmodium falciparum in liver cells.

More specifically, (I) corresponds to at least part of the **liver stage** specific antigen (LSA) gene (the specification includes sequences for the 3'-(1496bp) and 5'- ends (956bp) of this gene, together with the derived amino acid sequence).

USE/ADVANTAGE - (I) and Ab are useful in immunological diagnosis of malaria caused by P. falciparum, esp. by testing serum samples. They provide a more sensitive test than known methods. (I) can also be used in vaccines while Ab can be used therapeutically. Fragments of the nucleotide sequence can also be used diagnostically (as probe  
Dwg.0/10

L8 ANSWER 7 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
DUPLICATE 3

AN 1990:472305 BIOSIS

DN BA90:111725

TI SECONDARY STRUCTURE AND IMMUNOGENICITY OF HYBRID SYNTHETIC PEPTIDES  
DERIVED FROM TWO PLASMODIUM-FALCIPARUM PRE-ERYTHROCYTIC ANTIGENS.

AU LONDONO J A; GRAS-MASSÉ H; DUBÉAUX C; TARTAR A; **DRUILHE P**

CS DEP. MED. MOLECULAR PARASITOL., NEW YORK UNIV. MED. CENT., 341E 25TH ST.,  
NEW YORK, NY 10010.

SO J IMMUNOL, (1990) 145 (5), 1557-1563.

CODEN: JOIMA3. ISSN: 0022-1767.

FS BA; OLD

LA English

AB Multicomponent synthetic vaccines containing both B and T cell epitopes belonging to two different pre-erythrocytic Ag of Plasmodium falciparum are presented. In a di-component hybrid, a circumsporozoite T cell **epitope** and a peptide representing a **liver stage** -specific Ag were connected to obtain a reciprocal reinforcement of helical potentials. In a tri-component hybrid, a sequence corresponding to the circumsporozoite repeat tetrapeptide (NPNA) was tandemly synthesized on the N-terminal end of the di-component hybrid. Both hybrid molecules were able to adopt a partial helical conformation in water as determined by circular dichroism studies. To analyze if the different components were immunologically functional in these vaccines, mice bearing genetic backgrounds known to respond or not to the individual components were immunized with the hybrids. The tri-hybrid peptide showed a high immunogenic capacity as it elicited, in both H-2b and H-2k mice, high antibody responses against every separate individual sequence. Moreover, the antibodies induced by these conformationally restricted peptides were able to recognize the corresponding native proteins in the liver schizont

and the sporozoite surface. H-2d mice, in which the immune response to the individual components was genetically restricted, did respond against the di-hybrid peptide. The tri-hybrid peptide, in which NPNA repeats were present, lacked this H-2d-priming capacity but it triggered antibody production in H-2d mice previously primed with the di-hybrid peptide. These results indicate that multivalent vaccines can provide positive (potentiating) effects by carefully combining structurally well defined epitopes; however, negative (suppressive) effects are also possible suggesting that selection of multivalent vaccine components will require testing of combined molecules to optimize specific immune responses and avoid undesirable effects which may result from negative molecular interactions.

L8 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1989:551914 CAPLUS

DN 111:151914

TI Peptides of Plasmodium falciparum protein produced in hepatocytes for malaria diagnosis and vaccines

IN Marchand, Claudine; **Druilhe, Pierre**; Puijalon-Mercereau, Odile; Langsley, Gordon

PA Institut Pasteur, Fr.

SO PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8805785	A1	19880811	WO 1988-FR74	19880209
	W: AU, JP, US				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	FR 2610631	A1	19880812	FR 1987-1543	19870209
	FR 2610631	B1	19891124		
	AU 8813428	A1	19880824	AU 1988-13428	19880209
	AU 610571	B2	19910523		
	JP 01502194	T2	19890803	JP 1988-501827	19880209
	JP 2729070	B2	19980318		
	EP 343186	A1	19891129	EP 1988-901854	19880209
	EP 343186	B1	19930519		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	AT 89566	E	19930615	AT 1988-901854	19880209
	US 5599542	A	19970204	US 1988-275139	19881006
	US 5589343	A	19961231	US 1995-463512	19950605
PRAI	FR 1987-1543	A	19870209		
	EP 1988-901854	A	19880209		
	WO 1988-FR74	A	19880209		
	US 1988-275139	A3	19881006		

OS MARPAT 111:151914

AB Peptides or proteins comprising the sequence: Leu-Ala-Lys-Glu-Lys-Leu-Gln-X-Gln-Gln-Ser-Asp-Leu-Glu-Gln-Glu-Arg (I; X = Glu, Gly), or circular permutations of I are useful for tests and kits for diagnosing malaria and for vaccines. Peptides I are characteristic of a protein produced in hepatocytes infected with *P. falciparum*. A genomic DNA library of *P. falciparum* was constructed. Clones were screened against human antibodies specific for the hepatic stage; 3 expressed chimeric protein recognized by these specific antibodies and not by antibodies to other Plasmodium or to other stages of *P. falciparum*. The DNA sequence of clone DG 307 was detd. It contained a 51-base-pair repeat motif of I [I (X = Glu)-I (X = Glu)-I (X = Gly)-partial I (X = Glu)]. Clone DG 307 coded for the principal epitope of *P. falciparum* liver-specific antigen.

L8 ANSWER 9 OF 9 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN

AN 1987-12227 BIOTECHDS

second screening and the study of cross-reactions, several subsets of DNA clones expressing antigens present on the surface of sporozoites, or in liver stages, or in both, could be identified. In exposed individuals a high prevalence of antibodies to several of these antigens was found.

L11 ANSWER 10 OF 14 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

AN 95130823 EMBASE

DN 1995130823

TI Identification of conserved **antigenic** components for a cytotoxic T lymphocyte-inducing vaccine against malaria.

AU Aidoo M.; Lalvani A.; Allsopp C.E.M.; Plebanski M.; Meisner S.J.; Krausa P.; Browning M.; Morris-Jones S.; Gotch F.; Fidock D.A.; Takiguchi M.; Robson K.J.H.; Greenwood B.M.; **Druilhe P.**; Whittle H.C.; Hill A.V.S.; Good M.F.

CS Institute of Molecular Medicine, John Radcliffe Hospital, Oxford OX3 9DU, United Kingdom

SO Lancet, (1995) 345/8956 (999-1000+1003-1007).

ISSN: 0140-6736 CODEN: LANCAO

CY United Kingdom

DT Journal; Article

FS 004 Microbiology

026 Immunology, Serology and Transplantation

037 Drug Literature Index

LA English

SL English

AB Several cellular and humoral mechanisms probably play a role in natural immunity to Plasmodium falciparum malaria, but the development of an effective vaccine has been impeded by uncertainty as to which antigens are targeted by immune responses. Experimental models of malaria have shown that cytotoxic T lymphocytes (CTL) which kill parasite-infected hepatocytes can provide complete protective immunity against certain species of Plasmodium in mice, and studies in The Gambia have provided indirect evidence that CTL play a protective role against P falciparum in humans. By using an HLA-based approach, termed reverse immunogenetics, we have previously identified peptide epitopes for CTL in **liver-stage** antigen-1 and the circumsporozoite protein of P falciparum. We have extended this work to identify CTL epitopes for HLA class I antigens that are found in most individuals from Caucasian and African populations. Most of these epitopes are in conserved regions of P falciparum. CTL peptide epitopes were found in a further two antigens, thrombospondin-related anonymous protein and sporozoite threonine and asparagine rich protein, indicating that a subunit vaccine designed to induce a protective CTL response may need to include parts of several parasite antigens. However, CTL levels in both children with malaria and in semi-immune adults from an endemic area were low suggesting that boosting these low levels by immunisation might provide substantial or even complete protection against infection and disease.

L11 ANSWER 11 OF 14 CABA COPYRIGHT 2003 CABI on STN

AN 96:151043 CABA

DN 960805570

TI What vaccine for malaria?

Quel **vaccin** contre le paludisme?

AU **Druilhe, P.**; Perignon, J. L.

CS Laboratoire de Parasitologie Biomedicale, Institut Pasteur, 26, Rue du Dr Roux, 75015 Paris, France.

SO Archives de Pediatrie, (1996) Vol. 3, No. Suppl. 1, pp. 334s-335s.

Meeting Info.: XXXIe Congres de l'Association des Pediatres de Langue Francaise, Paris 1er-4 mai 1996.

ISSN: 0929-693X

DT Journal

LA French

Journal code: 2985117R. ISSN: 0022-1767.

CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Abridged Index Medicus Journals; Priority Journals  
OS GENBANK-S81602  
EM 199605  
ED Entered STN: 19960605

Last Updated on STN: 19980206

Entered Medline: 19960529

AB In the search for subunit vaccines that are able to induce the type of sterile, protective immunity achieved by irradiated sporozoites, there is increasing evidence that defense mechanisms directed at the intrahepatic stage and Ags expressed at this stage are critical. We have initiated a systematic search for such molecules and report here the identification and partial characterization of a novel Plasmodium falciparum gene encoding a 70-kDa protein, expressed in both sporozoite and liver stages (SALSA), with a vaccine potential that stems from its **antigenic** features. Antigenicity and immunogenicity studies were conducted in individuals exposed to malaria, in immunized mice, and in chimpanzees, using a recombinant protein and two synthetic peptides. Results show that the SALSA nonrepetitive sequence defines 1) major B cell epitopes, as shown by a high prevalence of Abs to each peptide in three African areas differing in their level of endemicity; 2) Th epitopes, as demonstrated by lymphoproliferation and IFN-gamma secretion in cells from the individuals from one of the low transmission areas, as well as helper effect upon Ab secretion in mice; and 3) epitopes for cytolytic lymphocytes, demonstrated in immunized and sporozoite-challenged chimpanzees, and associated with MHC class I leukocyte Ags. The latter are of particular importance, because this is the only part of the malaria life cycle in which the parasite is located in a cell expressing class I Ags and because CD8+ lymphocytes were found to be responsible for protection in experimental models.

L11 ANSWER 9 OF 14 MEDLINE on STN

AN 91243267 MEDLINE

DN 91243267 PubMed ID: 1709833

TI How to select Plasmodium falciparum pre-erythrocytic antigens in an expression library without defined probe.

AU Marchand C; **Druilhe P**

CS Parasitologie Biomedicale, Institut Pasteur, Paris, France.

SO BULLETIN OF THE WORLD HEALTH ORGANIZATION, (1990) 68 Suppl 158-64.

Journal code: 7507052. ISSN: 0042-9686.

CY Switzerland

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199107

ED Entered STN: 19910719

Last Updated on STN: 19960129

Entered Medline: 19910702

AB The restricted access to Plasmodium falciparum liver stages has greatly limited the analysis of the **antigenic** content of that stage. Due to the lack of material to perform immunochemical studies, of access to mRNA, and of monoclonal probes, we decided to screen a genomic library with stage-restricted human antibodies. This strategy led to the identification of a large number of DNA fragments encoding both sporozoite specific as well as **liver-stage** specific epitopes. Following the initial characterization of one **liver-stage** antigen, further screening was performed by using additional selective human antibodies. These were defined as having a high degree of reactivity with native antigens on either of the two stages while being negative with the already known molecules of the two stages. From this

USE - (A) are used to treat or prevent malaria, specifically where caused by Plasmodium falciparum.

ADVANTAGE - The combination of QS21 and 3D-MPL results in strong induction of a CS (circumsporozoite) protein-specific cytotoxic T cell (CTC) response, which is not generally induced by vaccines based on recombinant proteins, and synergistically increases production of gamma-interferon.

Dwg.0/4

L11 ANSWER 14 OF 14 LIFESCI COPYRIGHT 2003 CSA on STN

AN 93:33063 LIFESCI

TI How to select Plasmodium falciparum preerythrocytic antigens in an expression library without defined probe.

MALARIA VACCINE DEVELOPMENT: PRE-ERYTHROCYTIC STAGES.

AU Marchand, C.; Druilhe, P.; Hoffman, S.L. [editor]; Martinez, L.J. [editor]

CS Parasitol. Biomed., Inst. Pasteur, 25-28 Rue du Dr Roux, 75015 Paris, France

SO BULL. W.H.O., (1990) pp. 158-164.

Meeting Info.: Conference on Malaria Vaccine Development: Pre-erythrocytic Stages. Bethesda, MD (USA). 12-15 Apr 1989.

ISBN: 92-4-068680-0.

DT Book

TC Conference

FS K

LA English

SL English

AB The restricted access to Plasmodium falciparum liver stages has greatly limited the analysis of the **antigenic** content of that stage. Due to the lack of material to perform immunochemical studies, of access to mRNA, and of monoclonal probes, we decided to screen a genomic library with stage-restricted human antibodies. This strategy led to the identification of a large number of DNA fragments encoding both sporozoite specific as well as **liver-stage** specific epitopes. Following the initial characterization of one **liver-stage** antigen, further screening was performed by using additional selective human antibodies. These were defined as having a high degree of reactivity with native antigens on either of either of the two stages while being negative with the already known molecules of the two stages. From this second screening and the study of cross-reactions, several subsets of DNA clones expressing antigens present on the surface of sporozoites, or in liver stages, or in both, could be identified. In exposed individuals a high prevalence of antibodies to several of these antigens was found.